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DIELS-ALDER REACTIONS OF 1,2,3,6-TETRAHYDROBENZOCYCLOBUTENE-3,6-DIONES. A NEW SYNTHESIS OF [4.4.2]PROPELLANES AND A DIVERGENCE OF SITESELECTIVITY CONTROLLED BY STERIC HINDRANCE

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1,2,3,6-Tetrahydrobenzocyclobutene-3,6-diones underwent Diels-Alder reactions most preferably at the internal double bond giving [4.4.2]propellanes unless steric hindrance is not significant. The adducts with cyclic 1,3-dienes were transformed photochemically to novel strained cage molecules.

Diels-Alder reactions of *p*-benzoquinones and 1,3-dienes have been valuable in organic syntheses.[1] When quinones are substituted unsymmetrically, siteselectivity and regioselectivity in addition to stereoselectivity become matters of importance, and a number of investigations directed to the elucidation of such selectivities have been reported.[2]

Recently we have reported the synthesis of 1,2,3,6-tetrahydrobenzocyclobutene-3,6-dione (1) and some simple derivatives.[3] These quinones have two differently substituted double bonds, an internal ($C_{2a,6a}$) and an external ($C_{4,5}$) one. In view of enhanced dienophilicity of a strained double bond over an unstrained one, it might be expected that the strained internal double bond of 1 would show higher dienophilicity than the strain-free external one. On the contrary, however, the steric hindrance exerted by the four-membered ring should make the reaction at the internal double bond unfavorable (hereinafter cycloadducts at the internal and external double bond are termed internal adducts and external adducts, respectively). We wish here to report the results of Diels-Alder reactions of 1 and some derivatives with 1,3-dienes, which lead to a new synthesis of [4.4.2]propellanes (Tricyclo[4.4.2.$0^{1,6}$]dodecanes) and syntheses of novel strained cage molecules.

Table 1 summarizes the results of Diels-Alder reactions of 1 and a variety of 1,3-dienes.[4] As expected, quinone 1 reacted with butadienes 2a-e quite siteselectively giving internal adducts ([4.4.2]propellanes) 3a-e in good yields. These results sharply contrast with the result of reaction of nearly strain-free indan-4,7-quinone and 2,3-dimethylbutadiene 2e which yielded only an external adduct.[5] Even furan 2f, which does not give Diels-Alder adduct with *p*-benzoquinone itself, added to 1 at room temperature yielding again only internal adduct 3f stereoselectively. This may be ascribed to either the high dienophilicity of the internal double bond or the thermodynamic stability of 3f owing to release of strain.

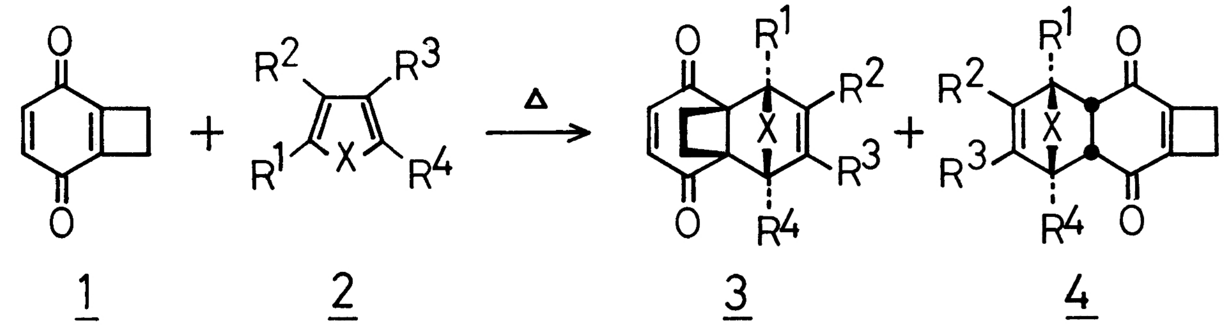
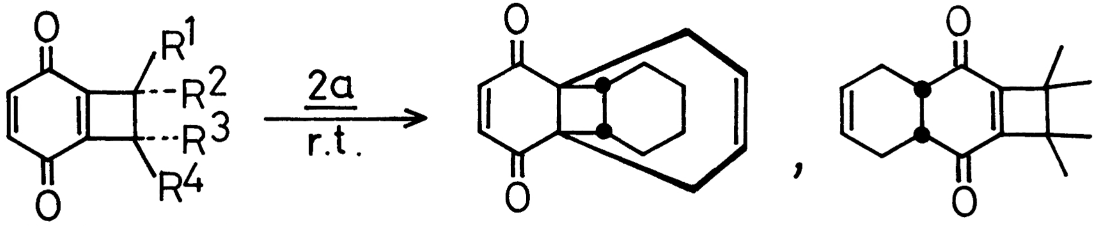


Table 1 Diels-Alder reactions of 1 and 1,3-dienes 2

	Dienes 2[a]					Coditions[b]		Internal Adducts 3		External Adducts 4	
	X	R^1	R^2	R^3	R^4	Temp. °C	Time hr	Yield%[c]	Mp°C	Yield%[c]	Mp°C
a	H,H[d]	H	H	H	H	r.t.	4	94	77-78	——	——
b	H,H[d]	CH_3	H	H	H	r.t.	4	87	96-98	——	——
c	H,H[d]	OAc	H	H	H	r.t.	4	84	88-90[e]	——	——
d	H,H[d]	H	CH_3	H	H	r.t.	10	77	oil	——	——
e	H,H[d]	H	CH_3	CH_3	H	r.t.	10	77	63-64	——	——
f	O	H	H	H	H	r.t.	48	85	140 dec	——	——
g	anthracene					80	20	83	225-226	——	——
h	C=O	Ph	Ph	Ph	Ph	80	6	87	208 dec	——	——
i	C=O	CH_3	Ph	Ph	CH_3[f]	80	0.5	81	197-199	13	155-157
j	CH_2	H	H	H	H	0	0.25	17[g]	168-170	83[g]	90-92
k	C◁	H	H	H	H	r.t.	2	——	——	89	128-130

[a] 1.2 equiv. of dienes were used except 2a, 2b, and 2d which were used in more excess because of their high volatility. [b] Dichloromethane (for 0°C and room temperature) or benzene (for 80°C) was used as the solvent. [c] Isolated yield after silica gel column chromatography unless otherwise stated. [d] 2a-e are 1,3-butadienes. [e] Almost single stereoisomer was obtained and the configuration of R^1 was tentatively assigned to be *anti* to the four-membered ring from steric point of view. [f] The dimer of this cyclopentadienone was used, which equilibrates with the monomer at the reaction temperature. [g] The ratio of 3j and 4j (determined from the ^1H NMR spectrum of the crude reaction mixture) is given because the latter compound tended to isomerize to the corresponding hydroquinone (mp 211-212°C) during chromatographic separation on silica gel.

Anthracene 2g and cyclopentadienones 2h and 2i showed similar siteselectivity. Cyclopentadiene 2j, however, yielded both internal adduct 3j and external adduct 4j in a ratio of 17:83. With spiro[2,4]hepta-4,6-diene 2k was obtained only external adduct 4k. These results indicate that, in addition to the dienophilicity of the double bonds, the steric interactions between X (and/or substituents nearby) of 2 and the cyclobutene moiety of 1 at the transition state play an important role in the siteselectivity. This is further supported by the reactions where steric factors are introduced in the cyclobutene of 1: while reaction of 1,2-tetramethylene derivative 5[3] with butadiene 2a still gave only internal adduct 6 (78%, mp 112-113°C), 1,1,2,2-tetramethyl derivative 7[3] did exclusively external adduct 8 (85%, mp 93-95°C). The relationship between the cyclohexane and the newly formed cyclohexene ring in 6 is probably *anti* with respect to the four-membered ring from steric point of view.



5: $R^1=R^4=H, -R^2-R^3-=-(CH_2)_4-$

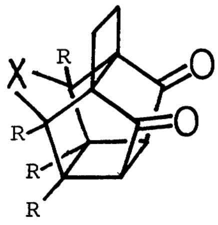
7: $R^1=R^2=R^3=R^4=CH_3$

6

8

The stereochemistrys of the adducts with cyclic dienes, 3 and 4, were established to be *endo* configuration by photochemical intramolecular [2+2] cyclization as described below. This configuration of 3f, 3h, 3i, and 3j accounts for the importance of the abovementioned steric interactions on the siteselectivity.

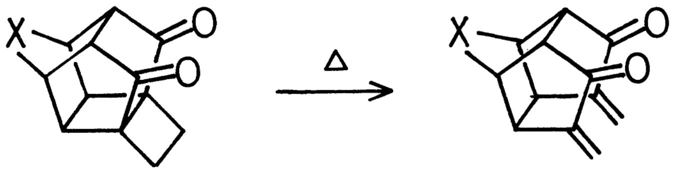
Photoirradiation of internal adducts 3f, 3h, and 3j in acetone or chloroform cleanly yielded cage molecules 9 (mp 261°C dec), 10 (mp 259°C dec), and 11 (mp 160°C dec), respectively. Similar irradiation of external adducts 4j and 4k formed another cage molecules 12 and 13 quantitatively (NMR analysis). While 9∿11 were relatively stable at room temperature, 12 and 13 had limited stability probably due to higher strain and underwent ring opening of the bicyclo[2.2.0]hexane moiety to give 14 and 15,[6] obeying the first order kinetics ($t_{1/2}$ of 12 at 34°C= ca 100 min).



9: X= O, R=H

10: X= C=O, R=Ph

11: X= CH_2, R=H



12: X=CH_2

13: X=C◁

14: X=CH_2

15: X=C◁

Some spectral data of the selected compounds are listed in Table 2.

Further sutdies on the properties of 1 and the cage molecules are in progress.

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Table 2 Some spectral data of selected compounds*

3a: ν_{max}(C=O) 1660 cm^{-1}; λ_{max} 220 (log ε 4.14), 385 nm (1.88); δ 1.9-2.7 (8H, m), 6.07 (2H, m), 6.83 (2H, s).

3f: δ 2.27 (4H, s), 5.13 (2H, br. s), 6.32 (2H, br. s), 6.65 (2H, s).

3g: δ 1.77 (4H, m), 4.73 (2H, s), 6.43 (2H, s), 6.9-7.6 (8H, m).

3j: ν_{max}(C=O) 1660 cm^{-1}; λ_{max} 222 (4.06), 390 nm (1.91); δ 1.4-2.4 (6H, m), 3.27 (2H, m), 6.02 (2H, t, J=1.8 Hz), 6.66 (2H, s).

4j: ν_{max}(C=O) 1664 cm^{-1}; λ_{max} 249 (4.04), 386 nm (1.77); δ 1.50 (2H, m), 2.82 (4H, s), 3.24 (2H, m), 3.54 (2H, m), 6.10 (2H, t, 1.8 Hz).

4k: δ 0.55 (4H, m), 2.83 (6H, m), 3.42 (2H, m), 6.22 (2H, t, 1.8 Hz).

6 : δ 1.0-1.9 (8H, m), 2.2-2.7 (6H, m), 6.10 (2H, m), 6.78 (2H, s).

8 : δ 1.30 (12H, s), 1.9-2.7 (4H, m), 3.24 (2H, m), 5.76 (2H, m).

9 : ν_{max}(C=O) 1730 cm^{-1}; δ 1.8-2.7 (4H, m), 2.97 (2H, m), 3.37 (2H, m), 5.07 (2H, (2H, m).

11: ν_{max}(C=O) 1734, 1717 cm^{-1}; δ 1.6-3.0 (10H, m), 3.17 (2H, m).

12 ν_{max}(C=O) 1740, 1718 cm^{-1}; δ 2.0 (2H, br. s), 2.1-2.9 (6H, m), 3.15 (4H, br. s).

14: ν_{max}(C=O) 1722 cm^{-1}; λ_{max} 212 (3.98), 234 (3.98), 340 (1.64), 354 nm (1.69); δ 2.06 (2H, m), 2.92 (4H, m), 3.35 (2H, m), 5.15 (2H, br. s), 5.97 (2H, br. s).

* IR spectra (ν_{max}) were taken in KBr disk, UV (λ_{max}) in cyclohexane, and ^{1}H NMR in CDCl$_3$ at 60 or 90 MHz using TMS as an internal standard.

References

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4. Satisfactory elemental analyses and/or mass spectra were obtained for all the new compounds described here.
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6. Although 14 and 15 are white solids, they did not show distinct melting or decomposition point and gradually colored above 200°C. Thermal behavior of these compounds are under investigation.

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